

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
10 September 2004 (10.09.2004)

PCT

(10) International Publication Number  
**WO 2004/075841 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K**
- (21) International Application Number:  
PCT/US2004/005265
- (22) International Filing Date: 23 February 2004 (23.02.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/449,629 24 February 2003 (24.02.2003) US
- (71) Applicant (for all designated States except US):  
**MALLINCKRODT INC.** [US/US]; 675 McDonnell  
Boulevard, P.O. Box 5840, St. Louis, MO 63134 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): **LIANG, Sidney**  
[US/US]; 1325 Arrowhead Drive, Olivette, MO 63132  
(US).
- (74) Agents: **BOONE, Jeffrey, S.** et al.; 675 McDonnell Boule-  
vard, P.O. Box 5840, St. Louis, MO 63134 (US).
- (81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.
- (84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-  
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,  
GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
ML, MR, NE, SN, TD, TG).
- Published:**  
— without international search report and to be republished  
upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: IMPROVED PROCESS FOR PREPARING BENZHYDRYLTHIOACETAMIDE

(57) Abstract: The present invention is directed to an improved process for preparing modafinil wherein benzhydrylthioacetamide is prepared in high yield and purity by the reaction of a haloacetamide with the reaction product of thiourea and benzhydrol in aqueous solution. The reaction employing the haloacetamide is conducted in a solvent comprising water and an organic solvent such as dimethylformamide having dissolved therein a basic salt such as potassium carbonate. The resulting benzhydrylthioacetamide can be oxidized to provide the pharmaceutical modafinil.